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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/752,415	01/06/2004	Bellon Laurent	MBHB00-885-E; 600.040	4210

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EXAMINER
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PITRAK, JENNIFER S

ART UNIT	PAPER NUMBER
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1609

SHORTENED STATUTORY PERIOD OF RESPONSE	MAIL DATE	DELIVERY MODE
3 MONTHS	03/15/2007	PAPER

**Please find below and/or attached an Office communication concerning this application or proceeding.**

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

# Office Action Summary

Application No.

10/752,415

Applicant(s)

LAURENT ET AL.

Examiner

Jennifer Pitrak

Art Unit

1609

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

## Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

## Status

- 1) ☒ Responsive to communication(s) filed on 06 January 2004.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

## Disposition of Claims

- 4) ☒ Claim(s) 1-28 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 1-28 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

## Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

## Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some \* c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
  - ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

## Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☒ Information Disclosure Statement(s) (PTO/SB/08)  
Paper No(s)/Mail Date 1/6/04
- 4) ☐ Interview Summary (PTO-413)  
Paper No(s)/Mail Date. \_\_\_\_\_
- 5) ☐ Notice of Informal Patent Application
- 6) ☐ Other: \_\_\_\_\_

## DETAILED ACTION

### *Claim Rejections - 35 USC § 112*

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter, which the applicant regards as his invention.

Claims 8 and 9 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claims 8 and 9 recite the limitation "said modified nucleotide". There is insufficient antecedent basis for this limitation in the claim.

### *Claim Rejections – Double Patenting*

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 1-4, 7, 10, 11, 13, 16, and 17 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over either of U.S. Patent No. 6,303,773 or U.S. Patent No. 6,162,909, in view of Wincott, *et al.* (BU). Claim 1 recites a process for synthesis, deprotection, and purification of an RNA molecule comprising solid phase oligonucleotide synthesis, one-pot deprotection, and purification. Claims 1, 7, and 8 of '773 are drawn to RNA synthesis on a solid support in a column and claims 1 and 10 of '909 are drawn to RNA synthesis on the surface of a well in a plate, both of which are "solid phase oligonucleotide synthesis" as claimed in the present application. The same claims of '773 and '909 are drawn to RNA deprotection "with a mixture of anhydrous alkylamine, trialkylamine, and a polar organic reagent in predetermined proportions" and contacting the deprotected RNA with "anhydrous triethylamine-hydrogen fluoride under conditions suitable for the removal of a 2'-OH protecting group." Claim 1 of the present application contains the same limitations first, by stating (in claim 1.b.i.) "alkylamine," which encompasses a mixture of anhydrous alkylamine and trialkylamine as claimed in '773 and '909, and second, by stating (in claim 1.b.ii.) "contacting the RNA with triethylamine-hydrogen fluoride," which encompasses "anhydrous triethylamine-hydrogen fluoride" as claimed in '773 and '909.

The claims of '773 and '909 do not teach the purification steps of the presently claimed method. However, in view of Wincott, *et al.* (BU), it would have been obvious to combine RNA synthesis and deprotection as claimed in '773 and '909 with purification as described in Wincott, *et al.* (p.2677, paragraph 2) which refers generally to the stepwise processes of RNA synthesis, deprotection, and purification. Furthermore, it was known by those skilled in the art that

Art Unit: 1609

synthesized RNA requires purification before it can be used. Also, in view of Wincott, *et al.*, the limitations of the present claims 2-4, drawn to HPLC purification comprising reverse phase and ion-exchange chromatography, are indicated in Wincott *et al.* in paragraphs 1 and 2 on p.2683 lines 5-9 as "...many methods exist for reversed phase HPLC (4,5,7) purification of oligonucleotides,..." and "Purification by anion exchange chromatography has been reported..." Thus, it would have been obvious to use reverse phase and/or ion-exchange HPLC for RNA purification as claimed in present claims 2-4. Claims 7, 10, 11, 13, 16, and 17 of the present application are rejected because the same limitations afforded by these claims are present in U.S. Patent '773 claims 3, 13, 19 and 20 and in U.S. Patent '909 claims 14-16.

Claims 5, 6, and 12 are rejected over claims 1, 7, and 8 of U.S. Patent No. 6,303,773 or claims 1 and 10 of U.S. Patent No. 6,162,909 in view of Wincott (BU) as applied above against claims 1-4, 7, 10, 11, 13, 16, and 17, further in view of Usman *et al.* (BQ). These claims describe the use of trialkylsilyl protecting groups and controlled pore glass for RNA synthesis. As was indicated above, the patent claims and Wincott (BU) teach the methods of claim 1. However, they do not teach the specific protective groups of the present claims 5 and 6 or the specific synthesis method of claim 12. Usman *et al.* describes the use of trialkylsilyl protecting groups such as triisopropylsilyl and *tert*-butyl dimethylsilyl on p.7846, paragraph 3 and on p.7848, Scheme II. Usman *et al.* also describes preparation of controlled-pore glass supports for RNA synthesis. It would have been obvious to combine the teachings of Usman, *et al.*, with the teachings of Patents '773, '909, and Wincott, *et al.* because, as described in the first sentence of Usman *et al.*, solid phase RNA synthesis requires protected ribonucleotides and controlled-pore glass supports.

Art Unit: 1609

Claim 14 is rejected over claims 1, 7, and 8 of U.S. Patent No. 6,303,773 or claims 1 and 10 of U.S. Patent No. 6,162,909 in view of Wincott (BU) as applied above against claims 1-4, 7, 10, 11, 13, 16, and 17, and over claims 1, 9, and 12 of U.S. Patent No. 6,054,576 in view of Usman *et al.* (BQ). Claim 14 specifies the removal of cyanoethyl protecting groups from synthesized RNA. As indicated above, the patent claims and Wincott (BU) teach the methods of claim 1 and claims 1, 9, and 12 of '576 teach the removal of phosphate protecting groups from synthesized RNA. The claims do not specifically teach cyanoethyl protecting groups.

However, cyanoethyl-protected phosphoramidites were evaluated as an alternative to methyl protecting groups in oligoribnucleotide synthesis as reported in Usman *et al.* (p.7848, column 2, first paragraph). According to Usman, *et al.*, the cyanoethyl protecting groups were easier to remove than methyl groups (abstract). Therefore, it would have been obvious to one skilled in the art at the time the present invention was made to use cyanoethyl protecting groups for RNA synthesis either as a comparable or improved reagent compared to the commonly used methyl protecting groups.

Claim 15 is rejected over claims 1, 7, and 8 of U.S. Patent No. 6,303,773 or claims 1 and 10 of U.S. Patent No. 6,162,909 in view of Wincott (BU) as applied above against claims 1-4, 7, 10, 11, 13, 16, and 17, and over claims 1, 9, and 12 of U.S. Patent No. 6,054,576 in view of Usman *et al.* (BO) and Wu, *et al.* Claim 15 specifies N-acetyl, N-benzoyl, or N-isobutyryl protecting groups. As indicated above, the patent claims and Wincott (BU) teach the methods of claim 1. However, they do not specify the type of RNA protecting groups. Wu, *et al.* (abstract) describe the improved chemical RNA synthesis with the use of the N-acetyl protecting group, phenoxyacetyl, for adenosine and guanine protection and furthermore, disclose that N-benzoyl

Art Unit: 1609

protecting groups remain adequate for cytidine nucleoside protection. Usman, *et al.* describe N-benzoyl and N-isobutyryl protecting groups in Figure 1. Therefore, given the evidence of successful use of these compounds in RNA synthesis, it would have been obvious to one skilled in the art to use these specific protecting groups (N-acetyl, N-benzoyl, and N-isobutyryl) in RNA synthesis.

Claims 18, 22, 24, 26, and 28 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 12, 15, and 16 of U.S. Patent No. 6,673,918 in view of Wincott, *et al.* (BU). Claim 18 describes a process for synthesis, deprotection, and purification of an RNA molecule comprising chemically modified nucleotides and claims 22, 24, 26, and 28 describe specific reagents and conditions for such a process. Claim 12 of '918 is drawn to one pot deprotection of RNA comprising modified nucleosides with the same limitations claimed in the present application claim 18.b. Claims 12, 15, and 16 of '918 teach the limitations of claims 22, 24, 26, and 28 of the present application. The claims of '918 do not teach the combination of RNA synthesis and purification with one-pot deprotection. Wincott, *et al.* refers generally to the stepwise process of RNA synthesis, deprotection, and purification (p.2677, paragraph 2). In view of Wincott, *et al.* (BU), in view of the fact that RNA deprotection would be necessary following synthesis, in which RNA protection is required, and in view of the general understanding of those skilled in the art that RNA purification is required for subsequent use of the RNA, it would have been obvious to combine RNA deprotection with synthesis and purification as described in Wincott (BU).

Claims 19, 20, 21, 23, 25, and 27 are rejected on the ground of nonstatutory obviousness-type double patenting as unpatentable over claims 12, 15, and 16 of U.S. Patent No. 6,673,918 in

Art Unit: 1609

view of Wincott, *et al.* (BU) as applied above against claims 18, 22, 24, 26, and 28 and over claims 1, 2, and 19 of U.S. Patent No. 6,303,773. As was indicated above, the patent claims and Wincott, *et al.*, teach the process of claim 18. Claim 19 of '773 teaches the modified nucleotides of the present claims 19-21, specifically 2'-deoxy-2'-fluoro, 2'-O'methyl, and 2'-deoxy nucleotides. Claims 1 and 2 of '773 disclose the process and reagent limitations presented in applicants' claims 23, 25, and 27. It would have been obvious to apply the limitations disclosed in '773 pertaining to deprotection of RNA to the deprotection of RNA after it has been synthesized, as claimed in the present application because both sets of claims are drawn to the very same process.

### ***Conclusion***


Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jennifer Pitrak whose telephone number is 571-270-3061. The examiner can normally be reached on Monday-Thursday, 7:30AM-5:00PM, ALT. Friday, EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Mary Mosher can be reached on 571-272-0906. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR

Art Unit: 1609

system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.



ZACHARIAH LUCAS  
PATENT EXAMINER